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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,282	04/14/2004	Donald Bellgrau	3921-1-1-1-1	7928

22442 7590 09/26/2008  
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EXAMINER
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KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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09/26/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/825,282	<b>Applicant(s)</b> BELLGRAU ET AL.	
	<b>Examiner</b> Sumesh Kaushal	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 54,55,64,66,68 and 69 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 54-55, 64, 66, 68 and 69 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's response filed on 07/09/08 has been acknowledged and fully considered.

*Claims 54-55, 64, 66, 68 and 69 are pending and are examined in this office action.*

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/09/08 has been entered.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 64, 66 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Arai et al (PNAS 94(25):13862-13867, 1997).

The instant claims are drawn to a method of inducing apoptosis in cancer cells by administering a viral vector encoding Fas Ligand. Arai et al teaches that gene transfer

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of Fas ligand induces tumor regression in-vivo. The cited art teaches that the Fas antigen is a cell surface receptor that transduces apoptotic signals into cells in response to the physiological ligand of Fas, Fas ligand (FasL), also known as CD95L or Apo-1L (page 13862, col.1). The cited art further teaches generation of recombinant ADV encoding FasL (ADV-FasL), see page 13863, col.1. The cited art further teaches regression of tumors after the ADV-FasL was injected into the tumors mediated (see page 13865, Fig 2 and 3). The cited art further teaches that human malignancies. HepG2 cells (HepG2), Hela cells (Hela), brain cancer (*three glioma cell lines G87, G138, and G373 and six melanoma cell lines M316, M342, M347, M444, M449, and M720*) express Fas and are susceptible to FasL mediated modulation (page 13866, fig-5). The cited art further teaches that FasL gene transfer can exert anti-tumor effects through two different mechanisms, either by induction of apoptosis through Fas-FasL engagement in Fas<sup>+</sup> tumors or through its ability to induce inflammation that is independent of Fas signaling to Fas<sup>-</sup> tumor cells. The cited art concluded that the ability to generate such potent inflammatory and apoptotic anti-tumor responses suggests that gene transfer of FasL may compensate for locally suppressive immune effects on tumor recognition and provide a useful molecular genetic intervention for malignancy (see discussion on pages 13865-67). Thus given the broadest reasonable interpretation the cited art clearly anticipates the invention as claimed.

### ***Claim Rejections - 35 USC § 112***

Claim 54-55, 64, 66, 68 and 69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing apoptosis in cancer cells in a solid tumor, does not reasonably provide enablement for a method of inducing apoptosis in cancer cells wherein the cancer cells are not in solid tumors (i.e . leukemia or lymphoma). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated earlier the specification (as filed) fails to teach induction of apoptosis in all kinds of tumors *especially systemic cancers (like leukemia eliciting tremendous metastatic potential)*, which would result in the reduction or elimination of tumor in-vivo. For example, the specification as filed fails to disclose the treatment of leukemia via method for gene therapy by systemic administration of Adenoviral vector comprising gene encoding CrmA and/or Fas- Ligand. The earlier office action provides clear evidence that cancer gene therapy is considered highly unpredictable. For example it is unclear how one skill in the art would target cancer cells circulating in the systemic circulation in view of applicant's disclosure and scope of invention as claimed.

In instant case treatment of any kind of cancer using any viral vector that encodes Fas-Ligand and CrmA via a method of gene therapy is not considered routine in the art and without an enabling disclosure the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

### **Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sumesh Kaushal  
Primary Examiner  
Art Unit 1633

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